Case No: HC03 CO3523

Neutral Citation Number: [2003] EWHC 3196 (Pat)
IN THE HIGH COURT OF JUSTICE
CHANCERY DIVISION
PATENTS COURT

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 12 December 2003

B e f o r e :

THE HONOURABLE MR JUSTICE LADDIE

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(1) WYETH HOLDINGS CORPORATION
(2) AHP MANUFACTURING B.V.
(3) JOHN WYETH & BROTHER LIMITED
(4) CYANAMID OF GREAT BRITAIN LIMITED **Claimants**

- and -

ALPHARMA LIMITED **Defendant**

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Mr Michael Tappin (instructed by **Linklaters** for the Claimants)
Mr Daniel Alexander QC and Ms Charlotte May (instructed by **Stephenson Harwood** for the Defendant)

Hearing dates: 11 & 12 December 2003

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JUDGMENT

Mr Justice Laddie:

1. This an application for an interim injunction. The claimant is Wyeth Holdings Corporation and a number of other companies in the Wyeth Group. I will refer to them all as Wyeth. The defendant is a company called Alpharma Limited ("Alpharma"). The claimants and the defendant are involved in the supply of pharmaceuticals to the English market.

2. The present dispute relates to the intention of Alpharma to start selling an antibiotic preparation in the UK, the active ingredient in which is a pharmaceutical called minocycline. That is an antibiotic which is related to tetracycline. Wyeth have been selling minocycline in the United Kingdom for some years under the trademark "Minocin-MR". The postscript " MR" refers to the fact that this is a modified release form of the drug. "Modified release" in turn refers to the way in which the drug is released from the capsule or tablet form in which it is swallowed by the patient as it makes its passage through the stomach, where there is an acid environment, into the intestine, where there is a more basic environment. What is needed is that at least some of the minocycline is released for absorption in the intestine.

3. Modified release minocycline is used to treat acne, a condition caused by infections of the skin by bacteria. It is particularly prevalent amongst young people. The Alpharma product in issue is sold under the trademark "Sebomin MR". It contains the same active ingredients as Minocin MR, that is to say minocycline, and is supposed to function in substantially the same way.

4. Minocycline had originally been introduced into the United Kingdom market by another company within the Wyeth Group pursuant to a marketing approval granted in November 1979. It was sold, I believe, in the form of simple yellow tablets. Wyeth carried out further research in relation to this antibiotic. Such research culminated in the application for, and subsequent granting of, patent EP0 310814, which I will refer to as "the Patent".

5. The Patent is entitled "Novel controlled release formulations of tetracycline compounds". As its name suggests, the invention is concerned with modifying the release characteristics of antibiotics. In particular, as I will explain below, it is concerned with modification of the release characteristics of minocycline. Modifying the release characteristics of pharmaceuticals may be of significance in the following circumstances: as mentioned above, when a pill or capsule is swallowed by a patient, it passes into the stomach and from there into the intestine. The contents of the stomach are acidic. On the evidence before me, the pH there can vary between about 1 and 3.5. The contents of the intestine are by comparison more alkaline exhibiting a pH normally of 4 or above. The average residence time of the contents of the stomach is about an hour, so a pill or capsule passes into an acidic environment and then into a more basic one. In some cases, it will be advantageous to reduce or eliminate acidic attack so that the pharmaceutical, or

at least more of it, survives passage through the stomach and into the intestine where it can be absorbed into the bloodstream.

6. The Patent is concerned with procuring such controlled release for minocycline. Minocin MR was given regulatory approval under a speedy procedure because of its relationship to the earlier minocycline products sold by Wyeth. It was placed on the market in this country in 1992 and has been sold by Wyeth ever since. Annual sales of Minocin MR have been substantial, but by comparison with many of the high-profile patented pharmaceuticals which come before these courts, still limited. The precise figure of sales is confidential and it is not necessary to refer to them in this judgment. For present purposes, it is sufficient to note that currently it returns to Wyeth several millions of pounds of gross profits each year, but the size of the market is sufficiently small that it may well attract competition from no more than one or two other suppliers.

7. Throughout the last ten years, Minocin MR has been sold in substantially the same get-up. The product is supplied to pharmacists in cardboard boxes which contain 56 Minocin MR capsules. Each box contains on it a number of dark blue or black panels on which the word "Minocin" is printed in white and the letters "MR" are printed in orange. Inside the box are blister packs, each of which contains 14 capsules. The blister packs are of common design, being plastic on one side and foil on the other. The foil is thin enough to be ruptured so that the capsules can be released one by one from the wells in the plastic part of the pack. On the foil side are printed the days of the week over each well. It also contains the words "Minocin MR".

8. The capsules within the blisters are in two colours: one end is orange; the other is dark brown. The word "Lederle" and a number are printed in white on the side of the capsules, but the writing is very small and not particularly noticeable.

9. I should mention that there is a good reason why the boxes contain 56 capsules. The treatment of acne involves administering one capsule each day for prolonged periods. Even if the course only lasts two months, 56 capsules will be needed. In fact, many patients are treated for much longer than this.

10. It appears that at some time in July this year, Wyeth learned of Alpharma's intention to put on the market its Sebomin product. It also contains minocycline. The product is also distributed in boxes containing 56 capsules in blister packs. The box used by Alpharma is quite different to that used by Wyeth. It has on it the words "Sebomin MR Capsules", and under this the words "Each modified release capsule contains 100mg anhydrous minocycline (as the hydrochloride)". Inside the box are four blister packs, each holding 14 Sebomin capsules. The design of the blister packs is also of the common sort, like that used by Wyeth on its product. However, it has printed on the foil side, besides the days of the week, the words "Sebomin 100mg MR capsules", under which is a reference to Alpharma. The blister pack also carries the letters "POM". This means that the product is a prescription-only medicine. As with Minocin MR, patients can only obtain these medicines if prescribed by a doctor.

11. Inside the Sebomin blister packs are the Sebomin capsules. They are substantially identical to the Minocin MR capsules. They use substantially the same shades of orange and brown. The only difference -- and it is not one which is likely to register with many patients -- is that the Sebomin capsules are marked at one end with a very small letter "C" and at the other end with a very small "MR".

12. On seeing the Alpharma product, Wyeth concluded that it infringed the Patent and that its sale or distribution would result in passing off. On 1 September this year, Wyeth's patent counsel wrote to Alpharma drawing the latter's attention to Wyeth's patents. In early September, Wyeth obtained a copy of Alpharma's price list, which indicated that Sebomin MR was being promoted as a substitute for Minocin MR.

13. It appears that Alpharma obtained regulatory approval for Sebomin on the basis that it was a controlled release version of minocycline, like Minocin MR. However, at an early stage during correspondence between the parties' respective solicitors, it was said on behalf of Alpharma that at a pH of 1.2, that is an acidity within the range of the pHs to be found in the stomach, the release of minocycline from the capsules was not retarded. For reasons which will be explained more fully later, Wyeth's solicitors believed that if this was true, and applied across the range of pHs to be found in the stomach, it would mean that there would be no infringement of the Patent. On the other hand, if so, it meant that Alpharma's product approval might have been obtained improperly, since that approval was for a modified release formulation.

14. As a result, Wyeth took steps towards pursuing judicial review proceedings. Those proceedings have been aborted by Wyeth. The reasons for doing so are not of significance to this application.

15. Alpharma had originally intended to launch Sebomin on 1st September this year. That launch was delayed a number of times. First, as a result of Wyeth's expressed concerns, it was put back from 1 September to 22 September, then again to 13 October. These proceedings were commenced on 7 October. Undertakings not to launch were given first to Mr Justice Patten on 10 October and then again to Mr Justice Neuberger on 22 October. Thus, the position now is that Alpharma has already held back its launch by some three and a half months.

16. Before me, Wyeth, represented by Mr Tappin, argues that there is an arguable case of infringement of the Patent and of passing off, and that the balance of convenience favours the grant of interim relief. Alpharma's response, as deployed by its counsel, Mr Alexander QC, was as follows: it said there was no strong or arguable case of infringement; the Patent was clearly either invalid or hopelessly weak; there was no serious case of passing off, and the balance of convenience favoured the refusal of an injunction.

17. Before turning to the Patent, I should say something about the defence, particularly as it relates to the Patent issues. Mr Alexander invites me to consider the validity of the Patent in the light of two pieces of prior art, namely US patent 4606909,

which I will refer to as Bechgaard, and a product called Doryx. In relation to the former, he said that his client had a very strong case of both anticipation and obviousness; in relation to the latter, he said he had a very strong case of obviousness. At least, that is what he suggested in his skeleton argument. Basing himself on my judgment in *Series Five Software* [1996] FSR 273, he said that I should assess the strength of the attack on the Patent and the arguments against infringement, and having concluded that, on both, Alpharma was likely to win, I should not grant interim relief.

18. I do not retract any of what I said in *Series Five Software*. If, at the interlocutory stage, it is clear to the court that one side's case is very strong and the other's is very weak, it should take that into account in deciding whether to grant relief. Indeed, it is common knowledge that in such cases the courts always do pay regard to the strength and weaknesses of the parties' cases. To do otherwise would be strange. However, this does not mean that it is proper for the court to engage in a mini-trial on written statements or for the parties to invite it to do so.

19. Most patent actions are too complicated to allow a court to reach a reliable view as to the merits at an interlocutory stage, and certainly not without engaging in a hard-fought mini-trial. *American Cyanamid v Ethicon* [1975] AC 396 illustrates only too clearly that, in such cases, the court should not try to determine the strength of the parties' respective cases. As long as the claims and defences are triable, it should move on to determining the balance of convenience.

20. There is nothing in this case which suggests that the court can or should try to come to a conclusion, particularly on the issue of validity, at this stage. Indeed, in my view, there are very good additional reasons why it should not be attempted here.

21. Neither side has filed any evidence from technical experts, either as to the meaning of technical words or on the issue of obviousness. Indeed, Mr Tappin protested that the first he or his clients knew that the issue of validity was to be argued on this application was when they received Mr Alexander's skeleton argument. Had they known that in this case, unlike other applications for interlocutory relief in patent cases, validity was going to be seriously argued, his clients would have put evidence before the court.

22. Mr Alexander's response to that was to say that the claimants were warned. In support of that, he relies on two paragraphs in the first witness statement of Mr Paul Fleming. Mr Fleming, it should be noted, is not put forward as a technical expert. He is the Director of Regulatory Affairs at Alpharma. At paragraphs 27 and 28, he says:

> "**Validity**.
>
> 27. Investigations are still continuing as to the prior art and other materials upon which Alpharma will rely to challenge the validity of the patent. If this claim is pursued Alpharma certainly intends to do so. Grounds of invalidity are due to be served on 3rd September and Alpharma is working with its advisers to meet that deadline.

> 28. There is now produced and shown to me, marked PAF 5, a copy of the EPO prosecution file for this Patent, of which a part is referred to in the defendants' Statement of Case on Construction and Infringement."

23. In no way is this a warning that validity would be argued seriously *on this application*. Mr Tappin's protest was justified.

24. There is an additional reason why the course pursued by Alpharma on this application was particularly inappropriate. Both Bechgaard and Doryx are referred to expressly in the discussion of prior art in the Patent. This must mean that the European Patent Office must have missed the blindingly obvious fact that the Patent was invalid in the light of these pieces of prior art. In my view, that was the essence of Mr Alexander's submission. Certainly, that was his approach to Bechgaard, which was the primary prior art he relied on during oral submissions.

25. In paragraph 20 of his skeleton, he said as follows:

> "Bechgaard was cited in the Patent and it is puzzling that the Patent was granted over it. The reason may lie in the representations made by the Patentee in the Patent itself as to how it was distinguishable. This may have diverted the EPO's attention."

26. The issue of obviousness was before the EPO and, after due consideration, it decided to grant the Patent. In my view, it is impossible for this court to assess the obviousness case at this stage particularly in the absence of any relevant evidence. Mr Tappin accepted that the obviousness attack was a real one, but he would go no further than that.

27. The same approach applies to the allegation of anticipation by Bechgaard. Indeed, if I were to venture a guess at this stage, I would say that this attack is likely to fail. The reason is simple: the claims in the Patent relate only to the manufacture of formulations containing minocycline. Bechgaard does not refer to minocycline at all. Mr Alexander says that it does refer to tetracycline, and that, because minocycline is a member of the tetracycline family, it must be covered by Bechgaard as well. I will assume, for this purpose, that all other features of the Patent claims are present in the prior art.

28. The trouble with this argument is, as noted already, there is no evidence as to the meaning of technical words before me. It follows that there is no basis upon which I could begin to conclude that the skilled reader of Bechgaard would see the word "tetracycline" and interpret it as covering not only tetracycline itself, but also a wide group of analogues. In fact, there are reasons for believing that the draftsman of Bechgaard had no such intention, but I do not need to explore those issues now.

29. It follows that I am not prepared to approach this application on any basis other than that the Patent is currently in force and that a non-demurrable attack on its validity is being run by Alpharma.

30. This takes me to the issue of infringement. The Patent teaches the reader how minocycline can be mixed with other ingredients, including excipients, extruded into a rotating device called a spheroniser, which, if run for long enough, will produce almost perfectly spherical pellets. These will give the necessary release characteristics if a suitable excipient is chosen.

31. I need only refer to claim 1, which reads as follows:

> "A pharmaceutical composition comprising granules which include in said granules an effective anti-bacterial amount of a 7- or 9-alkylamino-6-deoxy-6-demethyltetracycline or 1 a non-toxic acid addition salt thereof, blended with an effective amount of at least one pharmaceutically acceptable excipient, characterised in that said granules have the shape of spheres with a diameter of 0.1 to 2.5mm, obtained by spheronisation process, and are thereby adapted to retard the rate of release of said tetracycline compound in the human stomach and to promote rapid release of said tetracycline compound in the human intestine upon oral administration."

32. Four non-infringement arguments are run. First, it is said that Sebomin capsules do not contain spheres. Those capsules contain, what I will call "granules". Although those granules, which are made in a spheroniser, are within the size range of the claims, they are not spherical; they are lumpy. So, it is said, the product does not contain spheres as required in the claim.

33. This really does not admit of much argument. The word "sphere" in the claim cannot mean "perfect sphere". The question is, therefore: how far from the perfect sphere can one go before falling outside the claim? There is nothing in the specification which indicates that mis-shapen spheres will not work as well. So there is no indication of just how close to a perfect sphere one has to be to fall within the claim. Having looked at the contents of a number of Sebomin capsules, it appears to me perfectly arguable either that they contain a significant number of substantially true spheres or that their contents are sufficiently spherical to fall within the claim.

34. The second and third points relate to the words "Adapted to retard the rate of release ... in the human stomach and promote rapid release ... in the human intestine". Mr Alexander's two major points were as follows: (1) that at a pH of 1.2 there was no sufficient retard, and that that pH was the test set by the Patent; and (2), even at other pHs, the rate of release of minocycline from Sebomin in the acid environment of the stomach was faster than that in the intestine.

35. As to the first of these, I think there is force in Mr Tappin's argument that the Patent does not set a pH of 1.2 as a defining yardstick of the invention. The claim only

refers to the stomach which, as I have explained above, can have a pH which, from time to time, varies from 1 to 3.5. As far as the other point is concerned, again I think that Mr Tappin may well be right, that what is at issue is not the relative rate of release as between stomach and intestine, but whether release in the stomach is slowed, whether or not it is still faster than in the intestine, and whether, in the intestine, it is in fact fast enough to allow absorption. It must also be borne in mind that, if taken to its logical conclusion, this part of Alpharma's arguments leads one to wonder how Sebomin could be sold as modified release capsules.

36. The last point on non-infringement relates to the use of the word "thereby" in the claim. Mr Alexander says that the modified release characteristics must be due to the spheres. In Sebomin, he says, it is due to the choice of excipient or it has not been proved otherwise. Mr Tappin says that even if the excipient is relevant, its rate of release will be affected by the shape and composition of the spheres, and that is due to spheronisation. Further, he points out that the Patent itself makes clear that the choice of the right excipient is important. On this as on the other points, in my view, Mr Tappin has made out an arguable case of infringement.

37. As far as passing off is concerned, it appears to me to be very difficult to see the difference between this case and *Hoffman-La Roche v DDSA* [1969] FSR 410. In the end the crucial questions are: have Wyeth built up a valuable goodwill in their brown and orange capsules and, if so, will the use by Alpharma of the identical get-up lead to confusion and damage?

38. I can see little point in going through the issues in relation to passing off in detail, particularly in the light of my conclusion above, that Wyeth has an arguable case of patent infringement. Nevertheless, I think it at least arguable that Wyeth will be able to prove a protectable goodwill in its get-up as a result of its decade of selling Minocin capsules under this get up. Furthermore, it seems to me at least arguable that the adoption of the identical get-up by Alpharma will lead to a significant number of patients thinking they are getting the same again, meaning the same drug from the same source when they take Sebomin capsules. In coming to that conclusion, I do not ignore the differences in design of the outer boxes and blister packs. That Alpharma used the same get-up to reassure patients is not in dispute. Alpharma so asserts. It is at least arguable that part of that reasurrance would be as to source. It follows that an arguable case of passing off is made out.

39. The real question is what to do now. On the balance of convenience, fairly standard arguments were advanced. On the claimants' side, reliance was placed on the fact that the defendant, by its own admission, expects to take a very substantial part of its market by undercutting its price. It says it will be left with a stark choice of giving up a substantial market share or engaging in a price war. If, as is likely, the latter course is adopted, the price of the drug will be moved down and it will be impossible, in practice, to move it back up at a later date. Not only will there be a long-term loss of income, but it will be sizeable and will adversely affect Wyeth's ability to fund future research and development – just what patents are there for.

40. Mr Alexander explains that a price war is most unlikely. Although his client intends to undercut Wyeth's price, Wyeth would be ill-advised to retaliate because to do so would result in both companies doing worse than if Wyeth merely accepted, until the trial, loss of market share. Furthermore, Alpharma has not yet entered the market. If it succeeds at the trial, it will be very hard to calculate accurately how much market it would have captured had it not been injuncted at this stage.

41. As usual, there is much strength in these arguments. Whichever course I adopt will inflict significant damage on the losing party. That damage will never be fully assessable. However, in deciding what course to adopt, I think it is important to bear in mind that both parties agreed that this case could be ready for trial in about four months and are prepared to work to achieve that. It appears to me that the least unjust course will be to preserve the status quo pending the trial in April or May of next year. Alpharma has already put back the launch of this product by three and a half months. It appears to me that a bit of further delay should be tolerable. Furthermore, in relation to the passing off point, there is substance in Mr Tappin's argument that it has not been shown that any irreparable harm will be caused by the grant of an interim injunction in respect of this issue. Therefore, on any basis, existing stock will not be saleable and new product will have to be manufactured.

42. For these reasons I will grant the claimants the relief sought.